Remarks

The Office Action mailed July 30, 2007 has been carefully reviewed and the following response has been made in consequence thereof.

Claims 1-48, 55, and 56 are now pending in this application. Claims 1-56 stand rejected. Claims 49-54 have been canceled.

The objection to Claim 56 is respectfully traversed. Claim 56 has been amended to remove the multiple dependencies. Accordingly, Applicants respectfully request that the objection to Claim 56 be withdrawn.

The rejection of Claims 1-56 under 35 U.S.C. § 112, second paragraph, as being indefinite is respectfully traversed. Applicants have amended the claims to remove any grammatical and/or idiomatic errors. Accordingly, Applicants respectfully request that the Section 112 rejection of Claims 1-56 be withdrawn.

The rejection of Claims 1-19 and 55 under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting essential steps is respectfully traversed. Applicants have amended the independent claims to include all necessary steps for carrying out the invention. Accordingly, Applicants respectfully request that the Section 112 rejection of Claims 1-19 and 55 be withdrawn.

The rejection of Claims 1-56 as being unpatentable over Han et al. (Proc. Natl. Acad. Sci. USA, 1994) (hereinafter referred to as "Han") or Brugger et al. (Proc. Natl. Acad. Sci. USA, 1997) (hereinafter referred to as "Brugger") in view of Koivusalo et al. (J. Lipid Res., 2001) (hereinafter referred to as "Koivusalo") is respectfully traversed.

Han is cited for disclosing electrospray ionization mass spectroscopic analysis of human erythrocyte plasma membrane phospholipids involving linear regression analysis for correcting different instrumental efficiencies for molecular species. Brugger is cited for teaching quantitative analysis of biological membrane lipids at the low picomole level by nano-electrospray ionization tandem mass spectrometry. Koivusalo is cited for teaching

quantitative determination of phospholipid compositions by ESI-MS. However, none of these references describe or suggest generating a two dimensional plot identifying simultaneously multiple molecular ions of a lipid extract present on an x-axis and neutral loss or precursor ion scans of fatty acids of the lipid extract on a y-axis, and comparing peak heights for the molecular ions with that for an internal standard to identify and/or quantify hundreds to thousands of lipid and/or phospholipid molecular species.

Claim 1 recites a method for the determination of lipid individual molecular species composition of matter in a biological sample, said method comprising "subjecting the biological sample to lipid extraction to obtain a lipid extract . . . subjecting the lipid extract to two dimensional electrospray ionization tandem mass spectrometry (ESI/MS/MS) to generate at least one of a two dimensional plot and a multi-dimensional plot representing molecular ions of the lipid extract on a first axis and at least one of neutral loss scans of fatty acids of the lipid extract and precursor ion scans on a second axis . . . comparing peak heights for the molecular ions with that for an internal standard to at least one of identify and quantify the lipid molecular species."

Claim 1 is submitted to be patentable over Han or Brugger in view of Koivusalo. Specifically, none of Han, Brugger, or Koivusalo describe or suggest generating at least one of a two dimensional plot and a multi-dimensional plot representing molecular ions of a lipid extract on a first axis and at least one of neutral loss scans of fatty acids of the lipid extract and precursor ion scans on a second axis; and comparing peak heights for the molecular ions with that for an internal standard to at least one of identify and quantify the lipid molecular species.

Claims 2-7, 18, and 55 depend from independent Claim 1. When the recitations of Claims 2-7, 18, and 55 are considered in combination with the recitations of Claim 1, Applicants submit that Claims 2-7, 18, and 55 likewise are patentable over Han or Brugger in view of Koivusalo.

Claim 8 recites a method for the determination of lipid individual molecular species composition of matter directly from a lipid extract of a biological sample, said method

comprising "subjecting said lipid extract to electrospray ionization tandem mass spectrometry to generate at least one of a two dimensional plot and a multi-dimensional plot of molecular ions of the lipid extract versus at least one of neutral loss scans and precursor ion scans of lipid classes of the lipid extract . . . comparing peak heights for the molecular ions with that for an internal standard to identify and/or quantify the lipid molecular species."

Claim 8 is submitted to be patentable over Han or Brugger in view of Koivusalo. Specifically, none of Han, Brugger, or Koivusalo describe or suggest generating at least one of a two dimensional plot and a multi-dimensional plot of molecular ions of a lipid extract versus at least one of neutral loss scans and precursor ion scans of lipid classes of the lipid extract; and comparing peak heights for the molecular ions with that for an internal standard to identify and/or quantify the lipid molecular species.

Claims 9-17 depend from independent Claim 8. When the recitations of Claims 9-17 are considered in combination with the recitations of Claim 8, Applicants submit that Claims 9-17 likewise are patentable over Han or Brugger in view of Koivusalo.

Claim 19 recites a method for assessing a risk to an individual based on molecular species as an independent factor in the development of at least one condition in that individual for a medical condition selected from coronary artery disease, diabetes, stroke, atherosclerosis and obesity, wherein the method comprises "analyzing a biological sample taken of an individual for molecular species determination by comparing peaks heights of a plot of molecular ions of a lipid extract of the molecular species versus at least one of neutral loss scans and precursor ion scans of at least one of fatty acids and lipid classes that include constituents present in the lipid extract . . . administering a therapeutic amount of a drug to the individual . . . analyzing a corresponding biological sample of the individual . . . comparing the molecular species determination after drug administration with the molecular species determination prior to the drug administration . . . determining the benefit of decreased risk due to the drug now afforded to that individual."

Claim 19 is submitted to be patentable over Han or Brugger in view of Koivusalo. Specifically, none of Han, Brugger, or Koivusalo describe or suggest analyzing a biological

sample taken of an individual for molecular species determination by comparing peaks heights of a plot of molecular ions of a lipid extract of the molecular species versus at least one of neutral loss scans and precursor ion scans of at least one of fatty acids and lipid classes that include constituents present in the lipid extract.

Claims 20 and 56 depend from independent Claim 19. When the recitations of Claims 20 and 56 are considered in combination with the recitations of Claim 19, Applicants submit that Claims 20 and 56 likewise are patentable over Han or Brugger in view of Koivusalo.

Claim 21 recites a method for identifying an agent which selectively targets specific to at least one of a lipid and triacylglyceride molecular species, wherein the method comprises "analyzing a biological sample of at least one treated individual for molecular species or lipid molecular species determination by comparing peaks heights of a plot of molecular ions of a lipid extract of the molecular species versus at least one of neutral loss scans and precursor ion scans of the lipid extract . . . administering a drug to the individual . . . analyzing a biological sample from the individual . . . comparing the molecular species determination after said administration with the molecular species determination prior to drug administration . . . determining an effect on the individual of the drug administration."

Claim 21 is submitted to be patentable over Han or Brugger in view of Koivusalo. Specifically, none of Han, Brugger, or Koivusalo describe or suggest analyzing a biological sample of at least one treated individual for molecular species or lipid molecular species determination by comparing peaks heights of a plot of molecular ions of a lipid extract of the molecular species versus at least one of neutral loss scans and precursor ion scans of the lipid extract.

Claim 22 depends from independent Claim 21. When the recitations of Claim 22 are considered in combination with the recitations of Claim 21, Applicants submit that Claim 22 likewise is patentable over Han or Brugger in view of Koivusalo.

Claim 23 recites a method of identifying a candidate lipid modulating drug having lipid modulating drug efficacy, wherein the method comprises "analyzing a biological sample

of at least one individual subject for molecular species determination by comparing peaks heights of a plot of molecular ions of a lipid extract of the molecular species versus at least one of neutral loss scans and precursor ion scans of the lipid extract . . . administering a therapeutic amount of a candidate lipid modulating drug to the individual subject . . . analyzing a biological sample of the individual . . . comparing the molecular species determination after said administration with the molecular species determination prior to the drug administration . . . determining an effect if any on the individual of the drug administration."

Claim 23 is submitted to be patentable over Han or Brugger in view of Koivusalo. Specifically, none of Han, Brugger, or Koivusalo describe or suggest analyzing a biological sample of at least one individual subject for molecular species determination by comparing peaks heights of a plot of molecular ions of a lipid extract of the molecular species versus at least one of neutral loss scans and precursor ion scans of the lipid extract.

Claims 24 and 25 depend from independent Claim 23. When the recitations of Claims 24 and 25 are considered in combination with the recitations of Claim 23, Applicants submit that Claims 24 and 25 likewise are patentable over Han or Brugger in view of Koivusalo.

Claim 26 recites a method for diagnosing and determining the response of a patient to tailored drug therapy, wherein the method comprises "analyzing a biological sample of a patient to be treated or or other lipid molecular species determination by comparing peaks heights of a plot of molecular ions of a lipid extract of the molecular species versus at least one of neutral loss scans and precursor ion scans of the lipid extract . . . administering an amount of a drug to the patient . . . analyzing a biological sample taken from the treated patient . . . comparing the molecular species determination after the administration with the molecular species determination prior to the drug administration . . . determining an effect on the patient of the drug administration."

Claim 26 is submitted to be patentable over Han or Brugger in view of Koivusalo. Specifically, none of Han, Brugger, or Koivusalo describe or suggest analyzing a biological

sample of a patient to be treated or or other lipid molecular species determination by comparing peaks heights of a plot of molecular ions of a lipid extract of the molecular species versus at least one of neutral loss scans and precursor ion scans of the lipid extract.

Claim 27 depends from independent Claim 26. When the recitations of Claim 27 are considered in combination with the recitations of Claim 26, Applicants submit that Claim 27 likewise is patentable over Han or Brugger in view of Koivusalo.

Claim 28 recites a method of screening candidate chemicals for lipid modulating efficacy in a subject, wherein the method comprises "analyzing a biological sample of a subject for molecular species determination by comparing peaks heights of a plot of molecular ions of a lipid extract of the molecular species versus at least one of neutral loss scans and precursor ion scans of the lipid extract . . . administering a therapeutic amount of a drug to that biological subject . . . analyzing a biological sample of said subject . . . comparing the molecular species determination after said administration with the molecular species determination prior to the drug administration . . . determining an effect if any on the subject of the drug administration."

Claim 28 is submitted to be patentable over Han or Brugger in view of Koivusalo. Specifically, none of Han, Brugger, or Koivusalo describe or suggest analyzing a biological sample of a subject for molecular species determination by comparing peaks heights of a plot of molecular ions of a lipid extract of the molecular species versus at least one of neutral loss scans and precursor ion scans of the lipid extract.

Claim 29 depends from independent Claim 28. When the recitations of Claim 29 are considered in combination with the recitations of Claim 28, Applicants submit that Claim 29 likewise is patentable over Han or Brugger in view of Koivusalo.

Claim 30 recites a method of treating a subject comprising "analyzing a biological sample taken of that subject for lipid molecular species determination by the method by multidimensional ESI/MS and quantitative changes, wherein the biological sample is analyzed by comparing peaks heights of a plot of molecular ions of a lipid extract of the

molecular species versus at least one of neutral loss scans and precursor ion scans of the lipid extract."

Claim 30 is submitted to be patentable over Han or Brugger in view of Koivusalo. Specifically, none of Han, Brugger, or Koivusalo describe or suggest analyzing a biological sample taken of an individual for molecular species determination by comparing peaks heights of a plot of molecular ions of a lipid extract of the molecular species versus at least one of neutral loss scans and precursor ion scans of the lipid extract.

Claims 31 and 32 depend from independent Claim 30. When the recitations of Claims 31 and 32 are considered in combination with the recitations of Claim 30, Applicants submit that Claims 31 and 32 likewise are patentable over Han or Brugger in view of Koivusalo.

Claim 33 recites a medical treatment comprising "analyzing a biological sample taken of a subject for molecular analysis determination by multidimensional ESIMS and prescribing a therapy based on the determination, wherein the biological sample is analyzed by comparing peaks heights of a plot of molecular ions of a lipid extract of the molecular species versus at least one of neutral loss scans and precursor ion scans of the lipid extract."

Claim 33 is submitted to be patentable over Han or Brugger in view of Koivusalo. Specifically, none of Han, Brugger, or Koivusalo describe or suggest analyzing a biological sample taken of an individual for molecular species determination by comparing peaks heights of a plot of molecular ions of a lipid extract of the molecular species versus at least one of neutral loss scans and precursor ion scans of the lipid extract.

Claims 34 and 35 depend from independent Claim 33. When the recitations of Claims 34 and 35 are considered in combination with the recitations of Claim 33, Applicants submit that Claims 34 and 35 likewise are patentable over Han or Brugger in view of Koivusalo.

Claim 36 recites a method of customizing a drug therapy lipid for a subject, wherein the method comprises "analyzing a biological sample taken of the subject for molecular

species determination by multidimensional ESI/MS by comparing peaks heights of a plot of molecular ions of a lipid extract of the molecular species versus at least one of neutral loss scans and precursor ion scans of at least one of fatty acids and lipid classes that include constituents present in the lipid extract . . . customizing the subject's drug therapy based on the results of the molecular species determination and quantitative changes."

Claim 36 is submitted to be patentable over Han or Brugger in view of Koivusalo. Specifically, none of Han, Brugger, or Koivusalo describe or suggest analyzing a biological sample taken of an individual for molecular species determination by comparing peaks heights of a plot of molecular ions of a lipid extract of the molecular species versus at least one of neutral loss scans and precursor ion scans of at least one of fatty acids and lipid classes that include constituents present in the lipid extract.

Claim 37 depends from independent Claim 36. When the recitations of Claim 37 are considered in combination with the recitations of Claim 36, Applicants submit that Claim 37 likewise is patentable over Han or Brugger in view of Koivusalo.

Claim 38 recites a method of retarding, preventing, ameliorating or diagnosing disease in a subject based on lipid molecular species determination of a biologic sample of the subject, wherein the method comprises "analyzing a biological sample taken of a subject for molecular species analysis by multidimensional ESIMS determination associated with the disease by comparing peaks heights of a plot of molecular ions of a lipid extract of the molecular species versus at least one of neutral loss scans and precursor ion scans of at least one of fatty acids and lipid classes that include constituents present in the lipid extract . . . prescribing a therapy for the subject based on the alterations in the molecular species profiles of or other lipid molecular species after determination by multidimensional mass spectrometry."

Claim 38 is submitted to be patentable over Han or Brugger in view of Koivusalo. Specifically, none of Han, Brugger, or Koivusalo describe or suggest analyzing a biological sample taken of an individual for molecular species determination by comparing peaks heights of a plot of molecular ions of a lipid extract of the molecular species versus at least

one of neutral loss scans and precursor ion scans of at least one of fatty acids and lipid classes that include constituents present in the lipid extract.

Claim 39 depends from independent Claim 38. When the recitations of Claim 39 are considered in combination with the recitations of Claim 38, Applicants submit that Claim 39 likewise is patentable over Han or Brugger in view of Koivusalo.

Claim 40 recites a method of managing a library of chemicals, wherein the method comprises "administering a chemical selected from the library to a subject . . . analyzing a biological sample taken of that subject for lipid molecular species determination by multidimensional ESI/MS by comparing peaks heights of a plot of molecular ions of a lipid extract of the molecular species versus at least one of neutral loss scans and precursor ion scans of at least one of fatty acids and lipid classes that include constituents present in the lipid extract . . . quantitating the mass of individual entities . . . assigning a priority to said chemical for further development based on that determination."

Claim 40 is submitted to be patentable over Han or Brugger in view of Koivusalo. Specifically, none of Han, Brugger, or Koivusalo describe or suggest analyzing a biological sample taken of an individual for molecular species determination by comparing peaks heights of a plot of molecular ions of a lipid extract of the molecular species versus at least one of neutral loss scans and precursor ion scans of at least one of fatty acids and lipid classes that include constituents present in the lipid extract.

Claim 41 depends from independent Claim 40. When the recitations of Claim 41 are considered in combination with the recitations of Claim 40, Applicants submit that Claim 41 likewise is patentable over Han or Brugger in view of Koivusalo.

Claim 42 recites a method of determining a subject's response to administration of a drug, wherein the method comprises "administering a drug to the subject . . . analyzing a biological sample taken of a subject for lipid molecular analysis by multidimensional ESI/MS following said administration, molecular species and quantitation, wherein the biological sample is analyzed by comparing peaks heights of a plot of molecular ions of a lipid extract

of the molecular species versus at least one of neutral loss scans and precursor ion scans of at least one of fatty acids and lipid classes that include constituents present in the lipid extract."

Claim 42 is submitted to be patentable over Han or Brugger in view of Koivusalo. Specifically, none of Han, Brugger, or Koivusalo describe or suggest analyzing a biological sample taken of an individual for molecular species determination by comparing peaks heights of a plot of molecular ions of a lipid extract of the molecular species versus at least one of neutral loss scans and precursor ion scans of at least one of fatty acids and lipid classes that include constituents present in the lipid extract.

Claim 43 depends from independent Claim 42. When the recitations of Claim 43 are considered in combination with the recitations of Claim 42, Applicants submit that Claim 43 likewise is patentable over Han or Brugger in view of Koivusalo.

Claim 44 recites a method of providing a medical assessment to a subject, wherein the method comprises "analyzing a biological sample taken of a subject for lipid molecular analysis by multidimensional ESI/MS by comparing peaks heights of a plot of molecular ions of a lipid extract of the molecular species versus at least one of neutral loss scans and precursor ion scans of at least one of fatty acids and lipid classes that include constituents present in the lipid extract . . . providing an assessment to the subject based on that determination."

Claim 44 is submitted to be patentable over Han or Brugger in view of Koivusalo. Specifically, none of Han, Brugger, or Koivusalo describe or suggest analyzing a biological sample taken of an individual for molecular species determination by comparing peaks heights of a plot of molecular ions of a lipid extract of the molecular species versus at least one of neutral loss scans and precursor ion scans of at least one of fatty acids and lipid classes that include constituents present in the lipid extract.

Claim 45 depends from independent Claim 44. When the recitations of Claim 45 are considered in combination with the recitations of Claim 44, Applicants submit that Claim 45 likewise is patentable over Han or Brugger in view of Koivusalo.

Claim 46 recites a method of enhancing medical care provided to a subject, wherein the method comprises "analyzing a biological sample taken of a subject for or other lipid molecular analysis by multidimensional ESI/MS by comparing peaks heights of a plot of molecular ions of a lipid extract of the molecular species versus at least one of neutral loss scans and precursor ion scans of at least one of fatty acids and lipid classes that include constituents present in the lipid extract . . . providing a modulated therapy to the subject."

Claim 46 is submitted to be patentable over Han or Brugger in view of Koivusalo. Specifically, none of Han, Brugger, or Koivusalo describe or suggest analyzing a biological sample taken of an individual for molecular species determination by comparing peaks heights of a plot of molecular ions of a lipid extract of the molecular species versus at least one of neutral loss scans and precursor ion scans of at least one of fatty acids and lipid classes that include constituents present in the lipid extract.

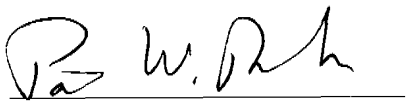
Claims 47 and 48 depend from independent Claim 46. When the recitations of Claims 47 and 48 are considered in combination with the recitations of Claim 46, Applicants submit that Claims 47 and 48 likewise are patentable over Han or Brugger in view of Koivusalo.

Claims 49-54 have been canceled.

For at least the reasons set forth above, Applicant respectfully requests that the Section 103 rejection of Claims 1-56 be withdrawn.

In view of the foregoing amendment and remarks, all the claims now active in this application are believed to be in condition for allowance. Reconsideration and favorable action is respectfully solicited.

Respectfully Submitted,



Patrick W. Rasche
Registration No. 37,916
ARMSTRONG TEASDALE LLP
One Metropolitan Square, Suite 2600
St. Louis, Missouri 63102-2740
(314) 621-5070